Electronic Supplementary Material 2

COST-EFFECTIVENESS OF CANAGLIFLOZIN ADDED TO STANDARD OF CARE FOR TREATING DIABETIC KIDNEY DISEASE (DKD) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) IN ENGLAND: ESTIMATES USING THE CREDEM-DKD MODEL

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AdViSHE Validation Assessment Tool:

The CREDENCE Economic Model of Diabetes Kidney Disease (CREDEM-DKD)
Version 1.1.1

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Part A: Validation of the Conceptual Model

- **A1:** Have experts been asked to judge the appropriateness of the conceptual model?

  Yes, the development of the conceptual model followed recommendations of the International Society of Pharmacoeconomic and Outcomes Research-Society of Medical Decision Making (ISPOR-SMDM) Modeling Good Research Practices Task Force-2 [1]. In addition to a literature review of economic models, expert clinicians were consulted to inform model design, objective, scope and key features, which was formally were documented in a conceptual model design. Consistent with the Task Force recommendations [1], the final conceptual design was not influenced by data availability. The final model conceptualization (and implementation) was examined by a multi-disciplinary NICE Scientific Advice Committee including a 3 hours face-to-face meeting.

- **A2:** Has this model been compared to other conceptual models found in the literature or clinical textbooks?

  Yes, the conceptual model was designed in part based on an initial pragmatic targeted literature review of existing economic simulation models of CKD and subsequently reviewed when a literature review that identified 101 models that included CKD was published in 2019 [2].

Part B: Input Data Validation

- **B1:** Have experts been asked to judge the appropriateness of the input data?

  Yes. The model was been presented to an associate Professor at University of Manitoba as well as to an inter-disciplinary team of clinical and modelling experts. The appropriateness of inputs used in CREDEM-DKD were discussed and changes were incorporated. UK-specific input data assumptions were reviewed by a NICE Scientific Advice Committee.

- **B2:** When input parameters are based on regression models, have statistical tests been performed?

  Yes. Regression models for the risk prediction equations are used in CREDEM-DKD. The regression models were first estimated with three parametric forms—exponential, Weibull, and Gompertz—and the functional form with best goodness-of-fit based on AIC was selected. Discrimination (C statistic) and calibration (ratio of predicted to observed cases at the study level, accounting for censoring on predictions using last outcome carried forward) were subsequently assessed, separately by study arm as well as overall.

Part C: Validation of the Computerized Model

- **C1:** Has the computerized model been examined by modeling experts?

  Yes. The model was been presented to an associate Professor at University of Manitoba as well as to an inter-disciplinary team of clinical and modelling experts. The appropriateness of the model was discussed and revisions were subsequently implemented.

- **C2:** Has the model been run for specific, extreme sets of parameter values in order to detect any coding errors?

  Yes. Every time a programing change is made to the model, implementation was tested systematically and debugged by both the programmer and other staff at the Swedish Institute for Health Economics. Formal verification tests of CREDEM-DKD have been conducted and are reported in AdViSHE Table 1. The methods are described in Willis et al. [3]

- **C3:** Have patients been tracked through the model to determine whether its logic is correct?

  Yes, CREDEM-DKD does not produce patient-level traces as standard outputs, health states and biomarker traces were generated and examined during model construction to confirm correct implementation.

- **C4:** Have individual sub-modules of the computerized model been tested?

  Yes. When model improvements were made to any sub-module, the modified sub-module was inspected thoroughly and tested with extreme sets of parameter values to isolate and investigate the effects of this sub-module on other parts of the model simulation.

Part D: Operational Validation

- **D1:** Have experts been asked to judge the appropriateness of the model outcomes?

  Yes. As part of developing of the conceptual design, a working group of health economists reviewed the evidence and met regularly with experts, conceptualizing the study problem and creating a preliminary statement of the study problem and the modeling objectives. In particular, CKD treatment guidelines, clinical evidence, and the CREDENCE study publications and data were consulted. Modeling guidelines were followed in the construction of the model, including the decision of what outcomes to report. The model was presented to a professor at the University of Manitoba as well as to an inter-disciplinary team of clinical and modelling experts. Furthermore, the final model conceptualization (and implementation) was examined by a multi-disciplinary NICE Scientific Advice Committee which included a 3-hour face-to-face meeting.

- **D2:** Have the model outcomes been compared to the outcomes of other models that address similar problems?

  No. As shown in the pragmatic literature review as well as the external model review, there are few models suitable for modeling the full set of kidney and macrovascular outcomes in T2DM patients with kidney disease. As such we have not been able to compare the model output to those of another model. We aim to cross-validate the model in the future when comparable models become available.

- **D3:** Have the model outcomes been compared to the outcomes obtained when using alternative input data?

  Yes. Model outputs generated using input data from a subset of the CANVAS Program participants [4] with characteristics that matched the CREDENCE trial [5] have been assessed and the results are presented in Willis et al.[3].

- **D4:** Have the model outcomes been compared to empirical data?

  Yes. Internal validation of CREDEM-DKD was performed by loading the model to replicate the CREDENCE study [5] (patient populations, treatment effects, and time horizon) and comparing model predictions of the cumulative incidence of the outcomes with the Kaplan-Meier curves from the CREDENCE trial. The Kaplan-Meier cumulative incidence curves describing internal model validation are presented in AdViSHE Figure 1. For additional details also see Willis et al.[3]. The model tended to overpredict the start of maintenance dialysis over the duration of the CREDENCE trial for both study arms, but the difference between arms was similar to that in the trial. The fit for the macrovascular and mortality outcomes were visually generally good.

External validation of CREDEM-DKD was performed by loading the model to replicate a subgroup of the CANVAS Program [4] with patient characteristics matching those of the CREDENCE study [5] and comparing model predictions of the cumulative incidence of the outcomes with the trial Kaplan-Meier curves. Note: as the CANVAS Program was designed to evaluate cardiovascular outcomes, start of maintenance dialysis was not recorded. The Kaplan-Meier results of the external validation using the subgroup of 567 patients in the CANVAS Program that met CREDENCE eligibility criteria [5] are presented in AdViSHE Figure 2. For additional details also see Willis et al.[3]. CREDEM-DKD overpredicted the incidence of doubling of serum creatinine in the CANVAS Program. Predictions for nonfatal myocardial infarction and hospitalization for heart failure visually matched CANVAS Program outcomes closely. The model also underpredicted all-cause mortality, especially after 1.5 years, and underpredicted the treatment effect. Ideally, external validation would have been conducted comparing versus a renal outcome trial, but none are available at this time. Several trials will report in upcoming years.

Part E: Other Validation Techniques

- **E1:** Have any other validation techniques been performed?

  No

References

1. Roberts M, Russell LB, Paltiel AD, Chambers M, McEwan P, Krahn M. Conceptualizing a model: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-2. Medical decision making : an international journal of the Society for Medical Decision Making. 2012 Sep-Oct;32(5):678-89.

2. Sugrue DM, Ward T, Rai S, McEwan P, van Haalen HGM. Economic Modelling of Chronic Kidney Disease: A Systematic Literature Review to Inform Conceptual Model Design. PharmacoEconomics. 2019 Sep 30.

3. Willis M, Asseburg C, Slee A, Nilsson A, Neslusan C. Development and Internal Validation of a Discrete Event Simulation Model of Diabetic Kidney Disease Using CREDENCE Trial Data. Diabetes therapy : research, treatment and education of diabetes and related disorders. 2020 Nov;11(11):2657-76.

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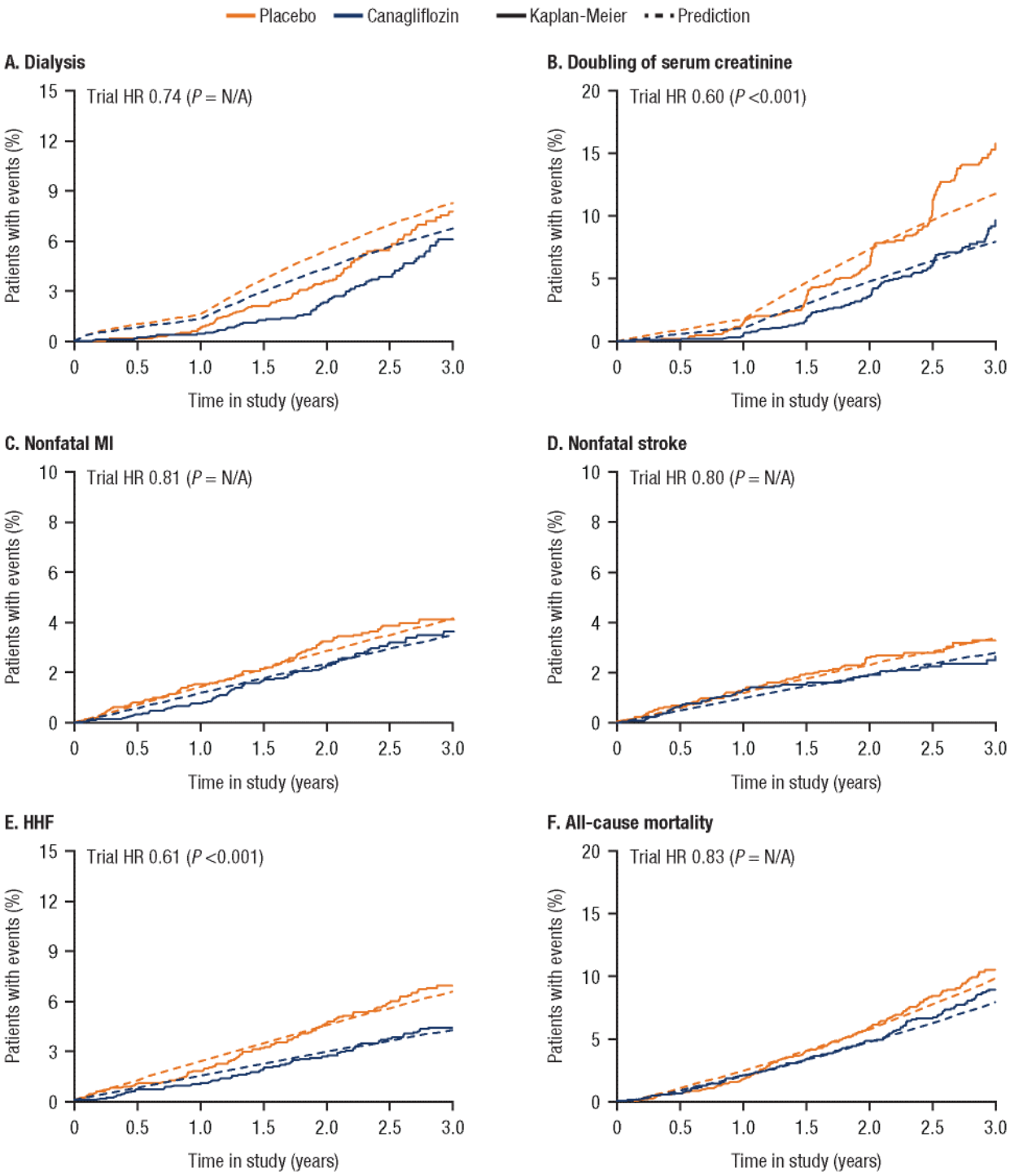
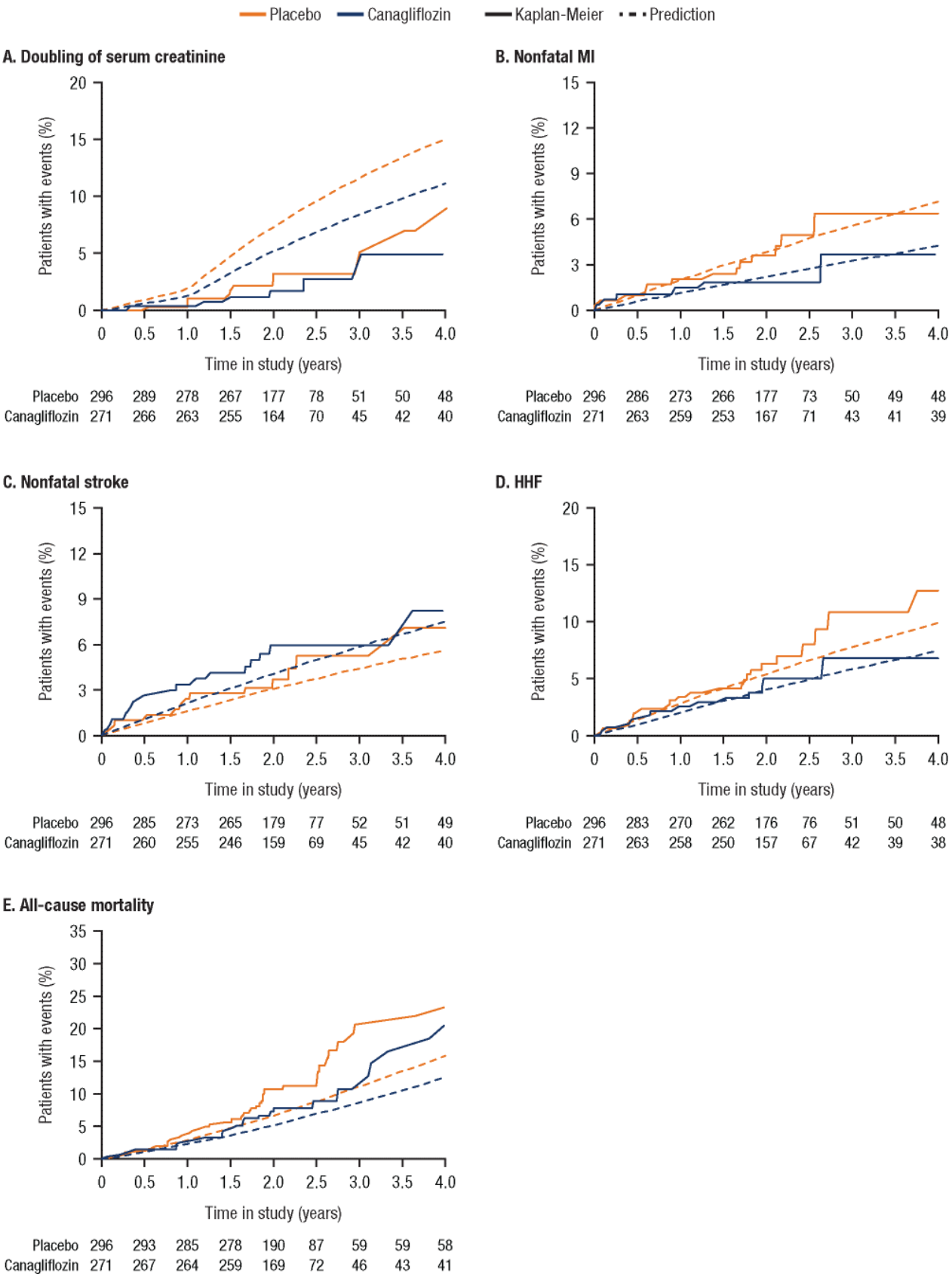
5. Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJL, Charytan DM, et al. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. The New England journal of medicine. 2019 Jun 13;380(24):2295-306.

Figure 1: Kaplan-Meier cumulative incidence curves for predicted and observed CREDENCE trial values, by outcome.



CREDENCE Canagliflozin and Renal Endpoints in Diabetes with Established Nephropathy Clinical Evaluation, HHF hospitalization for heart failure, HR hazard ratio, MI, myocardial infarction.

Figure 2: Kaplan-Meier cumulative incidence curves for predicted and observed CANVAS program subgroup values, by outcome.



CANVAS CANagliflozin cardioVascular Assessment Study, HHF hospitalization for heart failure, HR hazard ratio, MI, myocardial infarction.

Table 1: Stress-testing Overview

Scenario		Description	BC Value	Test value	Expected Outcomes	Results
Base Case	**BC**	--	--	--	(1) CV event rates should be lower in the intervention arm (2) Rates for dialysis and transplant should be lower in the intervention arm (3) CKD should progress over time with no regression of CKD (4) AE rates should be 0 in the comparator arm (5) CV mortality should be lower in the intervention arm (6) Procedural mortality should be lower in the intervention arm (7) Other cause mortality should be lower in the intervention arm (8) SoC costs should equal 100 X LY in the intervention arm	
transplant stage 5 pre-RRT	**T1**	Set an extremely high risk of transplant in stage 5 pre-RRT	Start eGFR: 55 Event rate pre-RRT: 0.1 Event rate post-RRT: 0.1	Start eGFR: 15 Event rate pre-RRT: 10000 Event rate post-RRT: 0	Everyone reaching the stage receives transplant, no-one progresses to dialysis, no costs for dialysis	Everyone reaching the stage receives transplant, no-one progresses to dialysis, no costs for dialysis
transplant stage 5 post-RRT	**T2**	Set an extremely high risk of transplant in stage 5 post-RRT, others to 0	Start eGFR: 55 Event rate pre-RRT: 0.1 Event rate post-RRT: 0.1	Start eGFR: 15 Event rate pre-RRT: 0 Event rate post-RRT: 10000 HR for dialysis set to 1000	Everyone reaching the stage receives transplant, no-one progresses to dialysis, no costs for dialysis	Everyone reaching the stage receives transplant, no-one progresses to dialysis, no costs for dialysis
transplant stage 5 pre-RRT	**T3**	Set low risk of transplant in stage 5 pre-RRT	Start eGFR: 55 Event rate pre-RRT: 0.1 Event rate post-RRT: 0.1	Start eGFR: 15 Event rate pre-RRT: 0 Event rate post-RRT: 0	No incidence of transplant, no costs for transplant	Extremely small event rates, cost indicate 1,47 events.
Minimum eGFR for transplant	**T4**	Minimum level set at 200	eGFR threshold: 10	eGFR threshold: 200 probability of transplant: 100%	Everyone receives transplant at simulation start, no start of dialysis	Everyone receives transplant at simulation start, no start of dialysis
Minimum eGFR for dialysis	**T5**	Minimum level set at 200	eGFR threshold: 10	eGFR threshold: 200 probability of transplant: 0%	Everyone receives dialysis at simulation start	Large amounts of dialysis at start

Scenario		Description	BC Value	Test value	Expected Outcomes	Results
Minimum eGFR for transplant	**T6**	Minimum level set at 0	eGFR threshold: 10	eGFR threshold: 0 probability of transplant: 100%	No start of transplant at simulation start	No start of transplant at simulation start
Minimum eGFR for dialysis	**T7**	Minimum level set at 0	eGFR threshold: 10	eGFR threshold: 0 probability of transplant: 0%	No start of dialysis at simulation start	No start of dialysis at simulation start
Minimum eGFR for death	**T8**	Minimum level set at 200	eGFR threshold: 5	eGFR threshold: 200	Everyone dies at simulation start	Everyone dies at simulation start
Minimum eGFR for death	**T9**	Minimum level set at 0	eGFR threshold: 5	eGFR threshold: 0	Results in line with BC	Results in line with BC
Extreme first year HRs mortality	**T10**	First year HR set to 0,000001	0.5	0.000001	Minimum amount of mortality in first year for intervention arm, PBO arm should be unaffected	Minimum amount of mortality in first year for intervention arm, PBO arm should be unaffected
Extreme first year HRs for mortality	**T11**	First year HR set to 100	0.5	100.0	High amount of mortality in first year for intervention arm, PBO arm should be unaffected	High amount of mortality in first year for intervention arm, PBO arm should be unaffected
Extreme first year HRs for other complications	**T12**	First year HR set to 0,000001	0.5	0.000001	Minimum number of events in first year, PBO arm should be unaffected	Minimum number of events in first year, PBO arm should be unaffected
Extreme first year HRs for other complications	**T13**	First year HR set to 100	0.5	100.0	Extreme number of events for intervention arm in first year, PBO arm should be unaffected	Extreme number of events for intervention arm in first year, PBO arm should be unaffected
No treatment effect in first year	**T14**	First year HR set to 1	0.5	1.0	Intervention arm follows comparator arm, PBO arm should be unaffected	Intervention arm follows comparator arm, PBO arm unaffected
Immediate cessation during simulation time	**T15**	Immediate secession set after year 1 and before simulation end	Inactive	Cessation after year 1	Event rates should be in line with PBO arm, Higher event rates than BC for intervention arm, PBO arm should be unaffected	Lower events in intervention arm in first year and then diminish difference between arms
Immediate cessation after simulation time	**T16**	Immediate secession set after year 100 and before simulation end	Inactive	Cessation after year 100	Same as BC	Same as BC
Fade-out during simulation	**T17**	Fade out effect at year 2 with a fade-	Inactive	Cessation after year 2 with fade-off set to 2 years	Lower event rates for intervention arm than in BC, PBO arm should be unaffected	Lower event rates for intervention arm than in BC, PBO arm should be unaffected

Scenario		Description	BC Value	Test value	Expected Outcomes	Results
		duration of 2 years				
Fade-out beyond simulation	**T18**	Fade out effect at year 2 with a fade-duration of 1000 years	Inactive	Cessation after year 2 with fade-off set to 1000 years	Results for intervention arm almost identical to those in BC and more favorable than results of Verification Test TX, PBO arm should be unaffected	Results for intervention arm almost identical to those in BC and more favorable than results of Verification Test TX, PBO arm should be unaffected
Fade-out after simulation	**T19**	Fade out effect starts after simulation ends	Inactive	Cessation after year 2 with fade-off set to 11 years	Same as BC	Same as BC
Intervention same as SoC	**T20**	Set intervention HR to 1	0.5	1.0	The results should be the same in both for both arms	Events same as Placebo
Active comparator	**T21**	Set active comparator effects to HR 1 and Intervention effects to HR 0.5	Intervention only	HR active comparator: 1.0 HR intervention: 0.5	The results should be the same as the BC for the intervention arm and the comparator arm	The results should be the same as the BC for the intervention arm and the comparator arm
Zero Values						
Progression	**T22**	Set progression to 0	As in CREDENCE	deactivated risk equations	No new events should occur	No events occurring
Pre-existing CV comorbidities	**T23**	Set pre-existing CV comorbidities to 0	CV history: 10%	CV history: 0%	State costs and disutility for CV events should be 0 in year one leading to less costs and QALYs CV compared to the BC in both arms	Less QALYs of CV compared to BC in both arms
Mortality	**T24**	Set mortality to 0	As in CREDENCE	Deactivated mortality	100% survival in both arms	Almost 100% survival, believe to be settings related
State and event costs	**T25**	Set all state and event costs to 0	Costs applied for events	No costs applied for events	Event and state costs should be 0	Event and state costs should be 0
Treatment costs	**T26**	Set treatment costs to 0	Treatment costs for intervention: 1 000	Treatment costs for intervention: 0	Treatment costs should be 0 in the intervention arm	Treatment costs should be 0 in the intervention arm
Treatment effects	**T27**	Set all HRs for the intervention	HR for intervention arm: 0.5	HR for intervention arm: 0.000001	In the Intervention arm: (1) almost 0 events should occur; (2) almost 0 event costs. In comparator arm: similar results as BC	As Expected,

Scenario		Description	BC Value	Test value	Expected Outcomes	Results
		arm to 0.000001				
Doubling of inputs		--				
Event rates	**T28**	Double all event rates	As in CREDENCE	Double the risk of events	Predicted events rates for HHF, MI, and stroke are doubled compared to BC	HHF & stroke doubled; MI substantially higher
Mortality	**T29**	Double mortality rate	As in CREDENCE	Double the risk of mortality	All-cause death is doubled compare to BC	All-cause death more than doubled compared to BC
State and event costs	**T30**	Double all state and event costs	Costs applied for events	Double costs applied for events	Event and state costs for CKD and CV should be doubled compared to BC	Event and state costs for CKD and CV doubled compared to BC
Treatment costs	**T31**	Double the treatment cost for intervention	Treatment costs for intervention/comparator: 1000	Treatment costs for intervention/comparator: 2000	Treatment cost for intervention doubled compared to BC	Treatment cost for intervention doubled compared to BC
Treatment effects	**T32**	Set all HRs for the intervention arm to 2	HR for intervention arm: 1.0	HR for intervention arm: 2.0	In intervention arm: (1) Even and CV/CKD mortality rates should be higher in the intervention arm; (2) Cost should be higher in the intervention arm; In comparator arm: similar results as BC	In intervention arm: (1) Even and CV/CKD mortality rates should be higher in the intervention arm; (2) Cost should be higher in the intervention arm; In comparator arm: similar results as BC
Baseline						
Age	**T33**	Set a low starting age	Starting age: 60(10)	Starting age: 40	(1) LY should be higher than BC	Higher LY than BC.
Age	**T34**	Set a high starting age	Starting age: 60(10)	Starting age: 80	(1) LY should be lower than BC	LY lower than BC.
Sex	**T35**	Set all patients to male	50% male/females	100% males	(1) LY should be lower vs BC	(1) LY lower vs BC
Sex	**T36**	Set all patients to female	50% male/females	100% females	(1) LY should higher vs BV	(1) LY higher vs BC
Smoking	**T37**	Set smoking status to 0%	10% Smokers	0% Smokers	(1) Lower LY vs BC	(1) Lower LY vs BC
Smoking	**T38**	Set smoking status to 100%	10% Smokers	100% Smokers	(1) Higher LY vs BC	Slightly lower LY vs BC
Diabetes Duration	**T39**	No diabetes duration	Diabetes duration 10(5)	Diabetes duration 0	(1) LY should be lower vs. BC (2) eGFR should decline more than BC	(1) LY lower vs. BC (2) very similar eGFR decline compared to BC

Scenario		Description	BC Value	Test value	Expected Outcomes	Results
Diabetes Duration	**T40**	Long diabetes duration	Diabetes duration 10(5)	Diabetes duration 20	(1) LY should be higher vs. BC (2) eGFR should decline less than BC	(1) LY higher vs. BC (2) very similar eGFR decline compared to BC
eGFR	**T41**	Set a low eGFR	Baseline eGFR: 55	Baseline eGFR: 30	(1) LY should be lower vs. BC (2) CV and CKD event should be higher vs. BC	LY lower than BC. CV and CKD event higher than BC
eGFR	**T42**	Set a high eGFR	Baseline eGFR: 55	Baseline eGFR: 90	(1) LY should be higher vs. BC (2) CV and CKD event should be lower vs. BC	(1) LY higher vs. BC (2) CV and CKD event lower vs. BC
log (UACR)	**T43**	Set a low log (UACR)	Baseline log (UACR): 6.5	Baseline log (UACR): 3	(1) LY should be higher vs. BC (2) DoSCR should be lower vs BC (3) Lower rates of CKD and CV event	(1) LY higher vs. BC (2) Lower rates of CKD and CV event. (3) DoSCr lower than BC
log (UACR)	**T44**	Set a high log (UACR)	Baseline log (UACR): 6.5	Baseline log (UACR): 9	(1) Lower LY vs BC (2) DoSCr rates should be higher vs BC (3) Higher rates of CV and CKD events	(1) Lower LY than BC. (2) DOSCr higher than BC. (3) higher event rates
Pre-existing CV comorbidities	**T45**	Set pre-existing CV complications to 100%	CV history: 10%	CV history: 100%	(1) LY should be lower vs BC (2) Costs should be greater vs. BC	(1) lower LY than BC (2) CV costs greater than BC, Higher costs in BC from treatment costs
Other logic tests						
State costs	**T46**	Set pre-existing CV complications to 100%, event and mortality rate to 0	CV history: 10% Risk: As in CREDENCE	CV history: 100% Mortality Intercept - 10,000	CV State costs should equal state costs for CV history times LY, should equal time horizon => (MI+stroke+HF) X LY => (500+500+500) X 10 =15,000	Approx. 15,000 (15,882)
Mortality	**T47**	Set mortality risk high	As in CREDENCE	Mortality intercept: 10,000	All-cause mortality should be almost 100% in year 1	Mortality at 100% at year 1
Slope effect eGFR	**T48**	Set slope to 0 for the intervention	Slope: 2.0	Slope: 0.0	(1) 100% of patients should be in Stage 5 at simulation start, (2) no progression should occur, (3) All patients should regress over time	100% of patients in Stage 5, patients regress over time
Slope effect eGFR	**T49**	Set slope to 100 for the intervention	Slope: 2.0	Slope: 100	Intervention group regress to Stage 1	Intervention group regress to Stage 1
Baseline CKD stage						
100% in stage 1	**T50**	Set baseline CKD stage to 100% in stage 1	Distribution between all CKD stages	eGFR 100	100% of patients should be in stage 1 at baseline, progression should occur over time	100% of patients should be in stage 1 at baseline, progression should occur over time

Scenario		Description	BC Value	Test value	Expected Outcomes	Results
100% in stage 2	**T51**	Set baseline CKD stage to 100% in stage 2	Distribution between all CKD stages	eGFR 75	100% of patients should be in stage 2 at baseline, progression should occur over time	100% of patients should be in stage 2 at baseline, progression should occur over time
100% in stage 3a	**T52**	Set baseline CKD stage to 100% in stage 3a	Distribution between all CKD stages	eGFR 52.5	100% of patients should be in stage 3a at baseline, progression should occur over time	100% of patients should be in stage 3a at baseline, progression should occur over time
100% in stage 3b	**T53**	Set baseline CKD stage to 100% in stage 3b	Distribution between all CKD stages	eGFR 37.5	100% of patients should be in stage 3b at baseline, progression should occur over time	100% of patients should be in stage 3b at baseline, progression should occur over time
100% in stage 4	**T54**	Set baseline CKD stage to 100% in stage 4	Distribution between all CKD stages	eGFR 22.5	100% of patients should be in stage 4 at baseline, progression should occur over time	100% of patients should be in stage 4 at baseline, progression should occur over time
100% in stage 5	**T55**	Set baseline CKD stage to 100% in stage 5	Distribution between all CKD stages	eGFR 5	100% of patients should be in stage 5 at baseline	100% of patients should be in stage 5 at baseline
Adverse events						
Once	**T56**	Set the occurrence for AE to Once	Recurrent AE	AE can only occur once	Less AE events/costs compared to BC in the intervention arm	Less AE events/costs compared to BC in the intervention arm
Permanent	**T57**	Set the occurrence for AE to permanent	Recurrent AE	AE are permanent	Less events but more costs related to AE compared to BC in the intervention arm	Less events but more costs related to AE compared to BC in the intervention arm
Stop treatment for AE A	**T58**	Set AE event rate for event A to 10 000, activate stop treatment for event A	Rate: 0.1 Stop treatment: No	Rate: 10 000 Stop treatment: Yes	(1) Intervention should be stopped almost immediately (2) The results should be the same in both treatment arms with the exception of AE-related results	No time on treatment, results similar. More transplants in intervention arm
Stop treatment for AE B	**T59**	Set AE event rate for event B to 10 000, activate stop treatment for event B	Rate: 0.1 Stop treatment: No	Rate: 10 000 Stop treatment: Yes	(1) Intervention should be stopped almost immediately (2) The results should be the same in both treatment arms with the exception of AE-related results	No time on treatment, results similar. More transplants in intervention arm

Scenario		Description	BC Value	Test value	Expected Outcomes	Results
Stop treatment for AE C	**T60**	Set AE event rate for event C to 10 000, activate stop treatment for event C	Rate: 0.1 Stop treatment: No	Rate: 10 000 Stop treatment: Yes	(1) Intervention should be stopped almost immediately (2) The results should be the same in both treatment arms with the exception of AE-related results	No time on treatment, results similar. More transplants in intervention arm
Stop treatment for AE D	**T61**	Set AE event rate for event D to 10 000, activate stop treatment for event D	Rate: 0.1 Stop treatment: No	Rate: 10 000 Stop treatment: Yes	(1) Intervention should be stopped almost immediately (2) The results should be the same in both treatment arms with the exception of AE-related results	No time on treatment, results similar. More transplants in intervention arm
Stop treatment for AE E	**T62**	Set AE event rate for event E to 10 000, activate stop treatment for event E	Rate: 0.1 Stop treatment: No	Rate: 10 000 Stop treatment: Yes	(1) Intervention should be stopped almost immediately (2) The results should be the same in both treatment arms with the exception of AE-related results	No time on treatment, results similar. More transplants in intervention arm
Discount rate	**T63**	Set discount rate to 10%	Discount rate: 0.0%	Discount rate: 10%	All costs should be less compared to the BC	All costs less compared to the BC
Time horizon 1 years	**T64**	Set time horizon to 1 years	Time horizon: 10 yrs.	Time horizon: 1 yr.	(1) Event/mortality rates should be lower than BC (2) LY should be less than 1 (3) costs should be less vs. BC	1) Events & Mortality lower than BC 2) LY less than 1. 3) Costs lower than BC.
Time horizon 5 years	**T65**	Set time horizon to 5 years	Time horizon: 10 yrs.	Time horizon: 5 yrs.	(1) Event rates should be similar to the BC (2) LY should be less than 5 (3) costs should be less vs. BC	Event rates similar to BC, LY < 5, costs lower than BC
Time horizon 20 years	**T66**	Set time horizon to 20 years	Time horizon: 10 yrs.	Time horizon: 20 yrs.	(1) Event rates should be similar to the BC (2) LY should be less than 20 (3) costs should be higher vs. BC	Approx. Similar event rates to BC, LY lower than 20, costs higher than BC
Costs						
Event costs	**T67**	Test Event Costs and Cum Incidence Match	BC Costs	Set all costs to 0. Then set event costs to1 for MI, HF, stroke, dialysis, and CV death. No discounting.	(1) Costs should match cumulative incidence for each of the selected outcomes	Cost matches

AE adverse event, BC base case, CKD chronic kidney disease, CREDENCE Canagliflozin and Renal Endpoints in Diabetes with Established Nephropathy Clinical Evaluation, CV cardiovascular, DKD diabetic kidney disease, DoSCr doubling of serum creatinine, eGFR estimated glomerular filtration rate, HF heart failure, HHF hospitalization for heart failure, HR hazard ratio, LY life-year, MI myocardial infarction, PBO placebo, SoC standard of card, UACR urine albumin:creatinine ratio